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OLFACTORY DISCRIMINATION AFTER DESTRUCTION OF THE ANTERIOR THALAMIC NUCLEI

K. S. LASHLEY AND R. W. SPERRY[1]

From Harvard University and the Yerkes Laboratories of Primate Biology

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The survey of forebrain structures by Swann (1935) and by Ghiselli and Brown (1938) has failed to reveal any structure essential for the olfactory discrimination between oil of anise and sheep dip (creosote). Allen (1941) has criticized this work on the ground that discrimination of these odors might be mediated alternatively by olfactory or trigeminal stimulation, but it should be emphasized that Swann was unable to obtain a discriminative reaction from any animal in which the olfactory bulbs had been destroyed. It seems certain that, in the concentrations used in his experiments, there was no differential trigeminal stimulation.

In a careful series of studies Allen (1941 and earlier) has reported effects upon olfactory reactions only after destruction of the frontal lobes or of the pyriform-amygdaloid complex in dogs. He concluded in summing up his work (1941) that disturbance of the relations between the pyriform-amygdaloid complex and the isocortex results in a loss of discriminative reactions and that the conditioned reaction to a single odor (presence vs. absence of odor) is probably mediated by impulses which pass to the cortex by way of the anterior thalamic nuclei (the principal path not explored in his experiments). It is not clear from his data that he obtained a true olfactory defect. On the contrary, the similarity of symptoms after frontal lobe and pyriform lesions and the indications of occasional discrimination by animals with such lesions suggest that he was dealing with a more general deterioration involving disturbances of the process of comparison, such as have been described after frontal and temporal lesions in monkeys.

Of cerebral systems intimately associated with primary olfactory centers, only the anterior nuclei have not been systematically investigated. Their cortical field is very extensive, including probably all of the infraradial and retrosplenial areas (Lashley, 1941) and the course of the projection fibers is such that the entire field has probably never been isolated from the thalamus in any experimental animal or clinical case. The present experiments were designed to test the effects of complete interruption of the radiations of the anterior nuclei upon a previously formed olfactory discriminative habit.

CORTICAL FIELD OF THE ANTERIOR NUCLEI. Three divisions of the anterior nucleus are distinguishable in the rat; the anterodorsal, anteroventral and anteromedial. The course and termination of their radiations has been described by Lashley (1941) on the basis of retrograde degeneration. The radiation of the anterodorsal nucleus passes forward around the fornix and through the callosal

[1] Fellow in Zoology, National Research Council.

fibers just in front of the thalamus to terminate in the Area retrosplenialis granularis. That of the anteroventral follows the same course, spreading more laterad, and terminates in the Area retrosplenialis agranularis. The radiation of the anteromedial nucleus passes forward along the mesial surface of the striatum to the Area infraradiata. The apparent course and termination of the fibers, as determined from lesions producing retrograde degeneration, are shown in figure 1. Section of the radiation results in complete disintegration of all neurons in the nucleus.

METHODS. *Animals.* Black female rats about five months old from a strain derived from a cross of albino with wild gray were used for the experiments.

Training. The apparatus used for training consisted of three small blocks of wood, each containing a well, 30 mm. in diameter and 40 mm. deep, provided

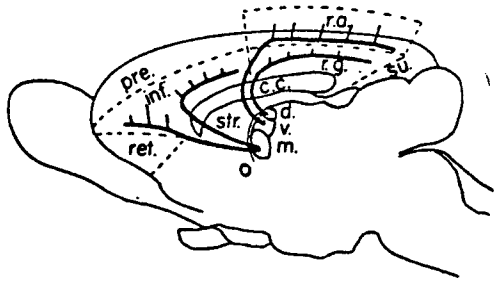

Fig. 1

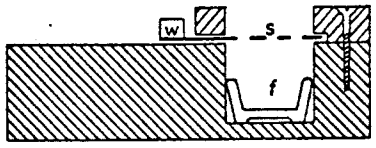

Fig. 2

Fig. 1. Diagram of the anatomic projection of the anterior nuclei upon the cerebral cortex. *d.*, anterodorsal nucleus; *v.*, anteroventral nucleus; *m.*, anteromedial nucleus; *c.c.*, corpus callosum; *inf.*, area infraradiata; *pre.*, regio praecentralis; *r.a.*, area retrosplenialis agranularis; *ret.*, regio retrobulbaris; *r.g.*, area retrosplenialis granularis; *str.*, corpus striatum; *su.*, area presubicularis. (Terminology of Rose, 1929.)

Fig. 2. Sectional sketch of one of the three training boxes. The circular well is closed by the perforated sliding cover, *s*, weighted by a small lead block, *w*. Food or cotton saturated with an odorous substance is placed in the glass dish, *f*, in the well. The rat opens the cover by clawing at the perforations above the well.

with a glass container at the bottom and with a perforated sliding metal cover which the rats could pull open (fig. 2). The blocks were impregnated and coated with paraffin so that they could be washed and recoated to remove odors. One block was placed in each of the three corners of a square restraining cage, 65 by 65 cm., and the rat admitted at the fourth. Milk-soaked bread was placed in one well and cotton with a few drops of oil of wintergreen in the others. The relative position of the blocks was varied in chance order in successive trials. The rats were given 5 to 10 trials per day until they chose the block containing bread and milk correctly in 28 or more of 30 consecutive trials (criterion of discrimination). Any attempt to open the cover of a well which did not contain food was counted as an error.

Controls. Reaction to position was controlled by chance arrangement of the relative positions in which the three blocks were placed. Non-olfactory cues

from the blocks were eliminated by regular washing and placing the food in each of the three in succession.

Oil of wintergreen is listed by Allen as a trigeminal irritant. Two controls were introduced to determine whether the rats were reacting to such stimulation and merely avoiding the wintergreen. *a.* Milk-soaked bread was added to the wells containing wintergreen after errorless performance had been established in operated animals. This led in every case to a confusion, with chance scores showing that the animals had been reacting to the food odor and that they could detect the food odor when mixed with wintergreen. *b.* When discrimination followed the cerebral operations, the animals were subjected to a second operation involving destruction of the olfactory bulbs. Total removal of the bulbs permanently abolished the discrimination, showing that the rats were not reacting to the trigeminal component of the wintergreen stimulation.

Operation. The animals were anesthetized with ether, the skull trephined near the midline on each side. A thermocautery was thrust diagonally downward and forward through the region of the genu to a sufficient depth to pass through the striatum, to sever the radiation of the anteromedial nucleus. A shallow transverse incision to the depth of the corpus callosum was also made above the septum to interrupt the radiations of the anterodorsal and anteroventral nuclei.

Analysis of lesions. At the termination of the experiment the brains were fixed in alcohol, sectioned and stained with thionin. With two exceptions, the animals had survived long enough to permit of total degeneration of injured cells, so that the boundaries of degenerated areas were clearly defined. Sections through the thalamus were examined for retrograde degeneration and camera lucida sketches made to show the approximate amount of degeneration in each nucleus.

EXPERIMENTAL RESULTS. Eight animals were carried through training, operation and postoperative tests. All gave evidence of retention of the discriminative reaction after operation. In five of the eight destruction of the radiation was incomplete so only the records of the three cases which are crucial for the problem will be reported.

No. 1. This animal made 37 correct choices in 38 trials after 15 trials of training. She was then rested ten days and given preoperative retention tests making no error. Operated and retested after 10 days, she gave 50 consecutive errorless trials in postoperative retention tests. The olfactory bulbs were then destroyed. Subsequent tests gave chance scores with no evidence of discrimination.

Sections showed total degeneration of the right anterodorsal, anteromedial and anteroventral nuclei. About 20 normal cells per section (less than 6 per cent of the normal number) were found in the left anterodorsal nucleus. The left anteroventral and anteromedial nuclei were totally degenerated. The nucleus reuniens was totally degenerated on both sides and the right and left dorsomedial nuclei showed some degeneration. The anterior half of the septum was destroyed and the third ventricle much distended.

No. 2. Thirty-seven of 38 trials were correct after 15 trials of training. Preoperative retention tests gave 10 consecutive errorless trials. She did not attempt to open the slides until the fourteenth day after operation, then gave 29 of 30 trials without error. The second operation, to destroy the olfactory bulbs, failed to remove the greater part of the left. Ensuing tests gave errorless performance for 3 days. The rat then developed an infection of the remaining bulb and the score fell to chance.

Sections showed total degeneration of the anterodorsal, anteroventral and anteromedial nuclei and of the nucleus reuniens on both sides. There was also extensive degeneration in the median division of the nucleus ventralis. The dorsal margin of the septum was destroyed.

No. 3. After 22 trials of training 40 errorless choices were made in 42 trials. The operation followed without the usual preoperative rest period. Following operation the animal had to be force-fed for several days and did not attempt to open the boxes until the twentieth day after operation. She then gave 39 correct responses in 42 trials. The olfactory bulbs were next destroyed. Subsequent training gave only 4 errorless in 40 trials, with no evidence of improvement.

Sections showed the anterodorsal, anteroventral, anteromedial and reuniens nuclei totally degenerated on both sides. The dorsal part of the medial division of the ventral nucleus and the mesial portion of the lateral nucleus also showed bilateral degeneration. The septum was entirely destroyed and there was slight invasion of the dorsal convexity of both hippocampal lobes.

These three cases give crucial evidence of the persistence of olfactory discrimination after interruption of the cortical radiations of the anterior nuclei. In numbers 2 and 3 all neurons of the anterior group had disappeared and in number 1 there were only a few possibly functional cells in the left anterodorsal nucleus. All of the animals discriminated accurately after the cerebral operation. Numbers 1 and 3 lost the habit after destruction of the olfactory bulbs and number 3 failed to reacquire it within twice the amount of training required for original learning. In number 2 the discrimination persisted after partial destruction of the olfactory bulbs but disappeared with infection of the remaining olfactory tissue. Thus it is clear that the discriminative reaction was mediated by the olfactory bulbs and that it was not abolished by total degeneration of all neurons in the three divisions of the anterior nucleus.

In the remaining five animals there was less extensive degeneration in the anterior nuclei, ranging from the persistence of a few normal cells in both anterodorsal nuclei to the preservation intact of one anteroventral nucleus. Their behavior was completely consistent with that of the three reported above.

DISCUSSION. By analogy with other senses one would expect to find an olfactory area in the isocortex essential for the most highly specialized discriminative reactions, with more primitive sensorimotor reactions mediated by thalamic or other subcortical mechanisms. The anatomic connections of the anterior thalamic nuclei have led Herrick (1931) and Kappers, Huber and Crosby (1936) to ascribe to these structures the correlation of olfactory with general somatic reactions. The cortical field of the anterior nuclei is extensive; equal

in area to the visual, auditory, or somesthetic fields, and has as yet no demonstrated function. There is therefore good reason to anticipate olfactory loss after total elimination of this system. The present experiments, however, have not revealed any disturbance of olfactory function after section of the radiation and total degeneration of the cells of the anterior nuclei. They suggest that the system is not involved in olfactory functions. It should be pointed out however, that the stimuli used were intense and perhaps simple. The olfactory apparatus of macrosmatic animals seems to be specialized for differentiation of organic odors to which man is relatively insensitive, and experiments with such substances as stimuli must be carried out before final conclusions concerning the olfactory functions of the anterior nuclear system are justified.

SUMMARY

Olfactory discrimination of rats was tested after interruption of the cortical radiations of the anterior group of nuclei. Discrimination between the odors of oil of wintergreen and of bread and milk was not disturbed by total bilateral degeneration of the anterodorsal, anteroventral and anteromedial nuclei, with additional involvement of the septum. Removal of the olfactory bulbs permanently abolished the discrimination, showing that the reaction was based upon olfactory and not trigeminal stimulation.

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